### (1) GENERAL INFORMATION:

- (i) APPLICANT: Hewick, Rodney M. Wang, Jack H. Wozney, John M. Celeste, Anthony J.
- (ii) TITLE OF INVENTION: Bone and Cartilage Inductive Proteins
- (iii) NUMBER OF SEQUENCES: 14
  - (iv) CORRESPONDENCE ADDRESS:
    - (A) ADDRESSEE: Legal Affairs, Genetics Institute, Inc.
    - (B) STREET: 87 CambridgePark Drive
    - (C) CITY: Cambridge
    - (D) STATE: MA
    - (E) COUNTRY: USA
    - (F) ZIP: 02140
    - (V) COMPUTER READABLE FORM:
      - (A) MEDIUM TYPE: Floppy disk
      - (B) COMPUTER: IBM PC compatible
      - (C) OPERATING SYSTEM: PC-DOS/MS-DOS
      - (D) SOFTWARE: PatentIn Release #1.0, Version #1.25
  - (vi) CURRENT APPLICATION DATA;
    - (A) APPLICATION NUMBER; US 07/800,364
    - (B) FILING DATE: 26-NOV-1991
    - (C) CLASSIFICATION:
- (viii) ATTORNEY/AGENT INFORMATION:
  - (A) NAME: Kapinos / Ellen J.

  - (B) REGISTRATION NUMBER: 32,245
    (C) REFERENCE/DOCKET NUMBER: GI 5182A
  - (ix) TELECOMMUNICATION INFORMATION:
    - (A) TELEPHONE 617-876-1170
    - (B) TELEFAX: /617-876-5851
- (2) INFORMATION FOR SEQ ID NO:1:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 23 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: unknown
  - (ii) MOLECULE TYPE: peptide
  - (iii) HYPOTHETICAL: NO
  - (iv) ANTI-SENSE: NO
  - (vi) /ORIGINAL SOURCE:
    - (F) TISSUE TYPE: Bone

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

Arg His Glu Leu Tyr Val Ser Phe Gln Asp Leu Gly Trp Leu Asp Trp 1 5 10 25

Val Ile Ala Pro Gln Gly Tyr
20

# (2) INFORMATION FOR SEQ ID NO:2:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 18 amino acids
  - (B) TYPE: amino acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: unknown
- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- (iv) ANTI-SENSE: NO
- (v) FRAGMENT TYPE: internal
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Bos taurus
  - (F) TISSUE TYPE: Bone
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

Leu Ser Ala Thr Ser Val Zeu Tyr Tyr Asp Ser Ser Asn Asn Val Ile 1 5 10 15

Leu Arg

#### (2) INFORMATION FOR SEQ/ID NO:3:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 7 amino acids
  - (B) TYPE: amino acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: unknown
- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- (iv) ANTI/SENSE: NO
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Bos taurus
  - (F) TISSUE TYPE: Bone
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

Ala Cys Cys Ala Pro Thr Lys

## (2) INFORMATION FOR SEQ ID NO:4:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 23 amino acids
  - (B) TYPE: amino acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: unknown
- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Bos taurus
  - (F) TISSUE TYPE: Bone
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO;

Thr Asn Glu Leu Pro Pro Pro Asn Lys Leu Pro Gly Ile Phe Asp Asp

Val His Gly Ser His Gly Arg 20

- (2) INFORMATION FOR SEQ ID NO:5:
  - (i) SEQUENCE CHARACTERISTACS:
    - (A) LENGTH: 80 base pairs

    - (B) TYPE: nucleic acid (C) STRANDEDNESS; double
    - (D) TOPOLOGY: limear
  - (ii) MOLECULE TYPE: DNA (genomic)
  - (iii) HYPOTHETICAL, NO
  - (iv) ANTI-SENSE NO
  - (vi) ORIGINAL/SOURCE:
    - (A) ORGANISM: Bos taurus
  - (vii) IMMEDIATE SOURCE: (B) /CLONE: acc30
  - (viii) POS/ITION IN GENOME:
    - (C) UNITS: bp
    - (ix) FEATURE:
      - (A) NAME/KEY: CDS
      - (B) LOCATION: 25..57
    - (ki) SEQUENCE DESCRIPTION: SEQ ID NO:5:

GGATCCGCGT GCTGTGCTCC GACC AAG CTG AGC GCC ACC TCC GTG CTC TAC Lys Leu Ser Ala Thr Ser Val Leu Tyr 1

TAC GAC AGCAGCAACA ATGTAATTCT AGA Tyr Asp 10

(2) INFORMATION FOR SEQ ID NO:6:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 11 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

Lys Leu Ser Ala Thr Ser Val Leu Tyr Tyr Asp 1 5 10

- (2) INFORMATION FOR SEQ ID NO:7:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 199 base pairs
    - (B) TYPE: nucleic acid
    - (C) STRANDEDNESS: double
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: DNA (genomic)
  - (iii) HYPOTHETICAL: NO
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Bos Taurus
  - (vii) IMMEDIATE SOURCE;
    - (A) LIBRARY: Bovine genomic
    - (B) CLONE: Lambda 9800-10
  - (viii) POSITION IN GENOME:
    - (C) UNITS: /bp
    - (ix) FEATURE:
      - (A) NAME/KEY: exon
      - (B) LOCATION: 30..199
    - (ix) FEATURE:
      - (A) MAME/KEY: intron
      - (B)/LOCATION: 1..29
    - (ix) FEATURE:
      - (A) NAME/KEY: CDS
      - (B) LOCATION: 30..179
    - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

TGCCCGCTGC CCCCTCCCGC CCCCGCCAG GTG CAC CTG CTG AAG CCG CAC GCG Val His Leu Lys Pro His Ala

GTC CCC AAG GCG TGC TGC GCG CCC ACC AAG CTG AGC GCC ACT TCC GTG 101 Val Pro Lys Ala Cys Cys Ala Pro Thr Lys Leu Ser Ala Thr Ser Val 10 CTC TAC TAC GAC AGC AGC AAC AAC GTC ATC CTG CGC AAG CAC CGC AAC 149 Leu Tyr Tyr Asp Ser Ser Asn Asn Val Ile Leu Arg Lys His Arg Asn 25 30 ATG GTG GTC CGC GCC TGC GGC TGC CAC TGAGGCCCCA ACTCCACCGG 196 Met Val Val Arg Ala Cys Gly Cys His CAG 199 (2) INFORMATION FOR SEQ ID NO:8: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 49 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear (ii) MOLECULE TYPE: protein (xi) SEQUENCE DESCRIPTION: SEQ ID NO:8: Val His Leu Leu Lys Pro His Ala Val Pro Lys Ala Cys Cys Ala Pro Thr Lys Leu Ser Ala Thr Ser Val Leu Tyr Tyr Asp Ser Ser Asn Asn Val Ile Leu Arg Lys His Arg Asm Met Val Val Arg Ala Cys Gly Cys His (2) INFORMATION FOR SEQ ID NO:9: (i) SEOUENCE CHARÁCTERISTICS: (A) LENGTH:/172 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: linear (ii) MOLECULE TYPE: DNA (genomic) (iii) HYPOTHÉTICAL: NO (vi) ORIGINAL SOURCE:

(A) ORGANISM: Bos taurus

(A) LIBRARY: Bovine genomic (B) CLONE: Lambda 9800-10

(vii) IMMEDIATE SOURCE:

(viii) POSITION IN GENOME: (C) UNITS: bp

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Asp Val His Gly Ser His Gly Arg Gln Val Cys Arg Arg His Glu Leu Tyr Val Ser Phe Gln Asp Leu Gly Trp Leu (2) INFORMATION FOR SEQ ID NO:13: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 1003 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: circular (ii) MOLECULE TYPE: cDNA to mRNA (iii) HYPOTHETICAL: NO (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo sapiens (F) TISSUE TYPE: Human Heart (vii) IMMEDIATE SOURCE: (A) LIBRARY: Human heart ODNA library stratagene catalog #936208 (B) CLONE: hH38 (viii) POSITION IN GENOME: (C) UNITS: bp (ix) FEATURE: (A) NAME/KEY: CDS (B) LOCATION: 8./850 (ix) FEATURE: (A) NAME/KEY: /mat\_peptide (B) LOCATION; 427..843 (ix) FEATURE: (A) NAME/KEY: mRNA (B) LOCATION: 1..997 (xi) SEQUENÇÉ DESCRIPTION: SEQ ID NO:13: GAATTCC GAG CCC CAT TGG AAG GAG TTC CGC TTT GAC CTG ACC CAG ATC 49 Glu Pro His Trp Lys Glu Phe Arg Phe Asp Leu Thr Gln Ile -135 -139/-130 CCG GCT GGG GAG GCG GTC ACA GCT GCG GAG TTC CGG ATT TAC AAG GTG 97 Pro Ala Gly Glu Ala Val Thr Ala Ala Glu Phe Arg Ile Tyr Lys Val -125 -120 CCC AGC/ATC CAC CTG CTC AAC AGG ACC CTC CAC GTC AGC ATG TTC CAG 145 Pro Ser Ile His Leu Leu Asn Arg Thr Leu His Val Ser Met Phe Gln -105 GTG FTC CAG GAG CAG TCC AAC AGG GAG TCT GAC TTG TTC TTT TTG GAT 193 Val /Val Gln Glu Gln Ser Asn Arg Glu Ser Asp Leu Phe Phe Leu Asp

-90

CTT (	CAG Gln	ACG Thr -75	CTC Leu	CGA Arg	GCT Ala	GGA Gly	GAC Asp -70	GAG Glu	GGC Gly	TGG Trp	CTG Leu	GTG Val -65	CTG Leu	GAT Asp	GTC Val	241
ACA (	GCA Ala -60	GCC Ala	AGT Ser	GAC Asp	TGC Cys	TGG Trp -55	TTG Leu	CTG Leu	AAG Lys	CGT Arg	CAC His -50	AAG Lys	GAC Asp	CTG Leu	GGA Gly	289
CTC ( Leu 1 -45	CGC Arg	CTC Leu	TAT Tyr	GTG Val	GAG Glu -40	ACT Thr	GAG Glu	GAT Asp	GGG Gly	CAC His -35	AGC Ser	GTG Val	GAT Asp	CCT Pro	GGC Gly -30	337
CTG (	GCC Ala	GGC Gly	CTG Leu	CTG Leu -25	GGT Gly	CAA Gln	CGG Arg	GCC Al'a	CCA Pro -20	CGC Arg	TCC	CAA Gln	CAG Gln	CCT Pro -15	TTC Phe	385
GTG (	GTC Val	ACT Thr	TTC Phe -10	TTC Phe	AGG Arg	GCC Ala	AGT Ser	CCG Pro -5	AGT Ser	CCC/ Pro	ATC Ile	CGC Arg	ACC Thr 1	CCT Pro	CGG Arg	433
GCA (																481
CCG (Pro (																529
CAC (	GGC Gly	CGG Arg	CAG Gln	GTC Val 40	TGC Cys	CGT Arg	ccc Arg	CAC His	GAG Glu 45	CTC Leu	TAC Tyr	GTC Val	AGC Ser	TTC Phe 50	CAG Gln	577
GAC (Asp )																625
TAT '																673
GCC A	ACC Thr 85	AAC Asn	CAC His	GCC Xla	ATC Ile	CTG Leu 90	CAG Gln	TCC Ser	CTG Leu	GTG Val	CAC His 95	CTG Leu	ATG Met	AAG Lys	CCA Pro	721
AAC Asn 100	GCA Ala	GTC Val	COC Pro	AAG Lys	GCG Ala 105	TGC Cys	TGT Cys	GCA Ala	CCC Pro	ACC Thr 110	AAG Lys	CTG Leu	AGC Ser	GCC Ala	ACC Thr 115	769
TCT (																817
CGC Arg	AAC/ Asn	ATG Met	GTG Val 135	GTC Val	AAG Lys	GCC Ala	TGC Cys	GGC Gly 140	TGC Cys	CAC His	TGA	GTCA	GCC (	CGCC	CAGCCC	870
TACT	<b>SCA</b>	GCC 2	ACCC'	rtct(	CA T	CTGG	ATCG	G GC	CCTG	CAGA	GGC	AGAA	AAC (	CCTT	AAATGC	930
TGTCACAGCT CAAGCAGGAG TGTCAGGGGC CCTCACTCTC GGTGCCTACT TCCTGTCAGG										990						

### (2) INFORMATION FOR SEQ ID NO:14:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 281 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:14

Glu Pro His Trp Lys Glu Phe Arg Phe Asp Leu Thr Gln Ile Pro Ala
-139 -135 -130 / -125

Gly Glu Ala Val Thr Ala Ala Glu Phe Arg/I/e Tyr Lys Val Pro Ser
-120 -115 -110

Ile His Leu Leu Asn Arg Thr Leu His Wal Ser Met Phe Gln Val Val -105 -100 -95

Gln Glu Gln Ser Asn Arg Glu Ser Asp Leu Phe Phe Leu Asp Leu Gln
-90 -85 -80

Thr Leu Arg Ala Gly Asp Glu Gly Trp Leu Val Leu Asp Val Thr Ala
-75 -65 -60

Ala Ser Asp Cys Trp Leu Leu Lys Arg His Lys Asp Leu Gly Leu Arg
-55 -50 -45

Leu Tyr Val Glu Thr Gly Asp Gly His Ser Val Asp Pro Gly Leu Ala
-40 -35 -30

Gly Leu Leu Gly Gln Arg Ala Pro Arg Ser Gln Gln Pro Phe Val Val

Thr Phe Phe Arg Ala Ser Pro Ser Pro Ile Arg Thr Pro Arg Ala Val

Arg Pro Leu Arg Arg Gln Pro Lys Lys Ser Asn Glu Leu Pro Gln
10 15 20

Ala Asn Ard Leu Pro Gly Ile Phe Asp Asp Val His Gly Ser His Gly 25 30 35

Arg Gln val Cys Arg Arg His Glu Leu Tyr Val Ser Phe Gln Asp Leu 45 50

Gly Trp Leu Asp Trp Val Ile Ala Pro Gln Gly Tyr Ser Ala Tyr Tyr

/55

60

65

Cys/Glu Gly Glu Cys Ser Phe Pro Leu Asp Ser Cys Met Asn Ala Thr 70 75 80 85

Asn His Ala Ile Leu Gln Ser Leu Val His Leu Met Lys Pro Asn Ala 90 95 100



51

Val Pro Lys Ala Cys Cys Ala Pro Thr Lys Leu Ser Ala Thr Ser Val

Leu Tyr Tyr Asp Ser Ser Asn Asn Val Ile Leu Arg Lys His Arg Asn 120 125 130

Met Val Val Lys Ala Cys Gly Cys His 135 140

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